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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/787,442

02/26/2004

Julia E. Novak

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ZYMOGENETICS, INC.
INTELLECTUAL PROPERTY DEPARTMENT
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EXAMINER

SEHARASEYON, JEGATHEESAN

ART UNIT

PAPER NUMBER

1647

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
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3 MONTHS

01/12/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No. 10/787,442	Applicant(s) NOVAK ET AL.	
	Examiner Jegatheesan Seharaseyon, Ph.D	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 October 2006.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2 and 10-12 is/are pending in the application.
 4a) Of the above claim(s) 3-9 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2 and 10-12 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 26 February 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>2/26/04 & 7/31/06</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Applicant's election without traverse of Group I a fusion polypeptide comprising a first polypeptide of SEQ ID NO: 2 and comprising a second polypeptide of SEQ ID NO: 111, drawn to claims 1 and 2 in the reply filed on 10/27/06 is acknowledged. Claims 10-12 drawn to the same elected invention have been added. Claims 3-9 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions of Groups II-VI, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 10/27/2006. Therefore, claims 1, 2 and 10-12 are pending and under consideration.

Drawings

2. The drawings filed 2/26/2004 are acknowledged.

Information Disclosure Statement

3. The IDS submitted 2/26/2004 and 7/31/2006 have been considered. Reference A3 in the IDS submitted 2/26/2004 is not found in the parent case (09/522217). Please provide a copy for consideration.

Specification

4. The use of the trademark Qiaquick (p. 71), gluta Max-I (p. 73), Fmax (p.74), Ficoll-Paque (p. 75), RNeasy Midi (p. 79), SuperscriptII (p.80), Pellet Paint (p. 81), ElectroMax (p.83), Nucleobond-giga (p.83), Super Broth (p.84) and lipofectamine (p.85) etc. have been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

5. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (p.101). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Objections

6. Claims 2 and 10 are objected to because of the following informalities:

6a. Claim 2 recites unelected inventions. Applicant is required to amend the claims to remove the unelected inventions.

6b. Claim 10 is objected to because the claim does not end with a period.

Appropriate correction is required.

Claim Rejections - 35 USC § 112, second paragraph

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 11 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7a. Claim 11 is rejected as vague and indefinite for reciting the term "the first polypeptide is sequence of amino acid residues as shown in SEQ ID NO: 2". It is unclear because the claim does not recite if "a sequence of amino acid residues" or "the

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sequence of amino acid residues" is desired. Therefore the metes and bounds of these claims are unclear.

Claim Rejections - 35 USC § 112, first paragraph

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8a. Claims 1, 2 and 10-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification while enabling for fusion protein comprising a first polypeptide of SEQ ID NO: 2 or a first polypeptide comprising residues 32 to 162 of SEQ ID NO: 2, does not reasonably provide enablement for all possible fusion proteins comprising a first polypeptide of at least 90% or 95% identical to SEQ ID NO: 2 or residues 32 to 162 of SEQ ID NO: 2 contemplated by the Applicant. The claims also recite the phrases "a sequence of amino acid residues" and thus, are broadly interpreted by the Examiner as reading upon: (i) protein variants with any number of deletions, substitutions, or additions and (ii) fragments of SEQ ID NOs: 2, including sequences only 6 amino acids in length (see specification page 55). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention as claimed.

The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. See *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the

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enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The instant claims reads on polypeptide sequence variants including those that are at least 90% or 95% identical to SEQ ID NO: 2 or polypeptide comprising residues 32 to 162 of SEQ ID NO: 2. The claims also recite the phrases "a sequence of amino acid" and thus, are broadly interpreted by the Examiner as reading upon: (i) protein variants with any number of deletions, substitutions, or additions and (ii) fragments of SEQ ID NOs: 2, including sequences only 6 amino acids in length (see specification page 55).

However, other than the polypeptide of SEQ ID NO: 2 or polypeptide comprising residues 32 to 162 of SEQ ID NO: 2, the specification as filed fails to disclose any other amino acid sequence recited in the instant claim. The specification does not teach functional or structural characteristics of the polypeptide variants, fragments, and derivatives encompassed by the claims.

Despite knowledge in the art for producing variant polypeptides, the specification fails to provide any guidance regarding the variant polypeptides contemplated that retain the function. Furthermore, detailed information regarding the structural and functional requirements of the disclosed protein is lacking. Although it is accepted that

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the amino acid sequence of a polypeptide determines its structural and functional properties, predicting a protein's structure and function from mere sequence data remains an elusive task. The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, *Biochemistry* 29:8509-8517; Ngo et al., 1994, *The Protein Folding Problem and Tertiary Structure Prediction*, pp. 492-495). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Although the specification outlines art-recognized procedures for producing and screening for active variants, this is not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further

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experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. Therefore, predicting which polypeptide, if any, would retain the functions of the protein is well outside the realm of routine experimentation. Further, since no function has been attributed to the claimed protein, the skilled artisan would not know what function to test for. Thus, an undue amount of experimentation would be required to generate the changes/modifications contemplated and yet retain the function of the proteins claimed.

Applicant has not taught how one of skill in the art would use the full scope of polypeptide sequences encompassed by the invention of claims 1, 2, 10 and 12. The specification as filed does not sufficiently teach one of skill in the art how to make and/or use the full scope of the claimed sequences. The amount of experimentation required to make and/or use the full scope of the claimed sequences would require trial and error experimentation to determine the functional sequences.

Given the breadth of claims 1, 2, 10 and 12 in light of the unpredictability of the art as determined by the lack of working examples and shown by the prior art of record, the level of skill of the artisan, and the lack of guidance provided in the instant specification, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention. Claim 11 is rejected insofar as it is depended on rejected claim 1.

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8b. Claims 1, 2 and 10 -12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *This is a written description rejection.*

The specification discloses the polypeptide of SEQ ID NO: 2 or polypeptide comprising residues 32 to 162 of SEQ ID NO: 2. This meets the written description provisions of 35 USC 112, first paragraph. However, the specification does not disclose all possible variants including those that are at least 90% or 95% identical to SEQ ID NO: 2 or polypeptide comprising residues 32 to 162 of SEQ ID NO: 2 contemplated by the Applicant. The claims also recite the phrases "a sequence of amino acid" and thus, are broadly interpreted by the Examiner as reading upon: (i) protein variants with any number of deletions, substitutions, or additions and (ii) fragments of SEQ ID NOs: 2, including sequences only 6 amino acids in length (see specification page 55).

The claims as written, however, encompass variant sequences which were not originally contemplated and fail to meet the written description provision of 35 USC 112, first paragraph because the written description is not commensurate in scope with the recitation of claims 1, 2, 10 and 12. The specification does not provide written description to support the genus encompassed by the instant claims.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116).

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With the exception of isolated polypeptide of SEQ ID NO: 2 or polypeptide comprising residues 32 to 162 of SEQ ID NO: 2, the skilled artisan cannot envision all the detailed chemical structure of the claimed polypeptide sequences of the variants regardless of the complexity or simplicity of the method of isolation.

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The polypeptide itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes v. Baird*, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class.

Therefore, only the fusion protein comprising a first polypeptide of SEQ ID NO: 2 or polypeptide comprising residues 32 to 162 of SEQ ID NO: 2 but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. As a result, it does not appear that the inventors were in possession of various polynucleotide sequences set forth in claims 1, 2, 10 and 12. Claim 11 is rejected insofar as it is depended on rejected claim 1.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.) Applicants are directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999.

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Double Patenting

9. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

9a. Claims 1, 2 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1, 2 of copending Application No. 11/ 551, 344. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

9b. Claims 1 is provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 1 of copending Application No. 11/ 551, 368. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

9c. Claims 1 is provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 1 of copending Application No. 11/ 551, 362. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims

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are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10a. Claims 1, 10 and 12 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4 of copending Application No. 11/551, 820 in view of Beckmann et al (U. S. Patent No. 5, 573, 924).

The instant invention discloses fusion protein comprising a polypeptide with at least 90% identity to a sequence of amino acid residues of SEQ ID NO: 2 or a first polypeptide comprising residues 32 to 162 of SEQ ID NO: 2 and comprising a second cytokine polypeptide or fragment thereof, wherein the fusion protein binds a receptor as shown in SEQ ID NO: 115. It does not teach a fusion protein with immunoglobulin heavy chain constant region as the second polypeptide.

Beckmann et al disclose soluble CD27L protein fusions where CD27 ligand protein is fused to immunoglobulin heavy chain constant region (column 6, lines 3-6). It also discloses fusion protein with Fc fragment (column 33-45). Therefore, it would have been *prima facie* obvious at the time of the invention to generate fusion protein comprising a polypeptide with at least 90% identity to a sequence of amino acid

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residues of SEQ ID NO: 2 or a first polypeptide comprising residues 32 to 162 of SEQ ID NO: 2 and immunoglobulin heavy chain constant region or Fc region because Beckmann et al. reference discloses the fusion proteins comprising the immunoglobulin heavy chain constant region. One of skilled in the art would have been motivated to generate the fusion protein comprising immunoglobulin molecule for use in purification, binding assays and screening. Therefore, the instant invention are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 10 and 12 of the instant invention in view of Beckmann et al (U. S. Patent No. 5, 573, 924).

This is a provisional obviousness-type double patenting rejection.

Relevant Art

11. Instant Application is a divisional of 09/522, 217 now U. S. Patent No. 6, 307, 024 (see PTO1449 of 7/31/2006), which discloses SEQ ID NO: 2 (Zalpha 11 ligand). Both Applications were filed Novak et al. Parrish-Novak et al. (2000) also disclose cytokine Zalpha 11 ligand (IL-21) of SEQ ID NO: 2 (see PTO1449 of 2/26/2004).

Conclusion

12. No claims are allowable.

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Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon, Ph.D whose telephone number is 571-272-0892. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JS
Art Unit 1647,
January 5, 2007

Jegatheesan Seharaseyon
Patent Examiner